REMARKS

Claims 1-40 were pending. The Examiner rejected claims 1-40 under 35 U.S.C. § 112, first paragraph; claims 33-40 under 35 U.S.C. § 112, first paragraph; and claims 1-10, 12 and 13 under 35 U.S.C. § 102(b). Applicants have herein amended claims 1, 9, 10, 14, 26, 27, 33, and 37; added new claims 41-50; and cancelled claims 7 and 24. Applicants' specification fully supports the new and amended claims (see, e.g., [0002], [0006], [0008], [0010], [0020], [0041], [0042], [0044], [0050], [0056], [0061], and [0063]). No new matter has been added. Accordingly, claims 1-6, 8-23, and 25-50 are pending.

In light of the amendments and the remarks herein, Applicants respectfully request reconsideration and allowance of claims 1-6, 8-23, and 25-50.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-40 under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. The Examiner concedes that the methods of making the claimed compounds are enabled by Applicants' specification, but asserts that the guidance provided by the specification in terms of enhancing cellular uptake at target cells invites further experimentation. In particular, the Examiner alleges that:

> the discovery that covalently conjugating pharmaceutically active compounds to guanidinoaminoglycosides results in enhanced cellular uptake of said active compounds would not have led a person having ordinary skill in the art to conclude that conjugating [any] beneficial compound by any means to any dialkoxy substance will also result in enhanced cellular uptake.

Applicants' respectfully disagree. The test of enablement is whether the specification teaches one skilled in the art how to make and use the full scope of the claimed invention without *undue experimentation*. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993) (emphasis added). Thus, the enablement analysis must be focused on the product or method defined by the claims. Importantly, "a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph *unless* there is reason to doubt the objective truth of

the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 439 F.2d 220, 222-223 (CCPA 1971) (emphasis in the original). The Examiner bears the burden of "providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement." *In re Wright*, 999 F.2d at 1561 (Fed. Cir. 1993). The Examiner has not met his burden in the present case.

Claim 1, as amended, recites a composition comprising a therapeutically active compound covalently bonded to an adduct of a dialkoxy substance and a guanidinylating reagent. The Examiner argues that while methods of making the claimed compounds are enabled by Applicants' specification, the methods of using the compounds invite further experimentation. As stated in MPEP § 2164.06, however, the test for enablement is "not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04 (CCPA 1976)). Applicants' respectfully assert that the present specification provides such guidance. For example, paragraphs [0072] to [0074] (methods for making and evaluating labeled conjugates) and Examples 10 and 11 provide examples of experiments which can be used to evaluate the cellular uptake of the claimed conjugates. Example 11, in particular, describes a method of evaluating the cellular uptake of an AZT-guanidino-neomycin B conjugate.

Moreover, methods for evaluating the activity of therapeutically active compounds both prior to conjugation to the adduct and after covalent bonding to the adduct are well known to those of skill in the art. Thus, one of skill in the art would know how to evaluate the activity of the covalently conjugated compound to determine whether the activity and/or cellular uptake of the therapeutically active compound have been altered. Accordingly, given the guidance in Applicants' specification and the knowledge of a person having ordinary skill in the art at the time of the filing of the present application, one of skill in the art would understand how to use the full scope of the claims without undue experimentation.

In light of the above, Applicants' respectfully assert that the present claims are enabled by the specification as filed and request withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

The Examiner also rejected claims 33-40 under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. The Examiner argues that the linker in claims 33-40 is not described in the specification with respect to the full scope of the claims. In particular, the Examiner alleges that the specification describes only specific linkers bound to specific compounds while the instant claims encompass a much broader genus of compounds and linkers.

Applicants respectfully disagree. The present specification, in combination with the knowledge of one of ordinary skill in the art, fully describes the claims. Written description is a question of fact, judged from the perspective of one of ordinary skill in the art. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Compliance with § 112 requires sufficient information in the specification to show that the inventor possessed the invention as of the relevant filing date. See *Vas-Cath*, 935 F.2d at 1563-64 ("[T]he applicant must . . . convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention."); *Union Oil Co. of Cal. v. Atl. Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000) ("The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'" (citation omitted)).

According to MPEP § 2164.04, a description is presumed adequate, unless or until the Examiner has presented sufficient evidence to rebut the presumption. See, e.g., *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971). The initial burden is therefore on the Examiner to present a reasonable basis to challenge the adequacy of the written description. This burden requires the presentation of a preponderance of evidence detailing why a person skilled in the art would not recognize that Applicant's disclosure adequately details the invention as described in the claims. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976). Applicants respectfully assert that the Examiner has not met his burden.

Claims 33-40 and 43-50 recite linkers which may be used to join a therapeutically active compound and an adduct. Examples and descriptions of such linkers are provided in Applicants' specification and include releasable linkers, thiol linkers, amine linkers, amino acid linkers, and hydrolysable linkers. See, e.g., paragraphs [0051], [0053], [0054], [0056], [0058], [0061] -

[0063], and [0065]. Moreover, specific examples of linkers are also provided, including dithiols such as β-mercapto-ethylether (see [0063]) and amino acids such as glycine (see [0061]).

As described in paragraph [0065] of Applicants' specification and would be understood by one of skill in the art, the linker of the instant claims may be tuned based on the desired composition and use of the conjugate. The use of linkers to covalently bond two components is well-known in the art and the description provided in Applicants' specification clearly indicates to one of skill in the art that Applicants have invented the full scope of the pending claims.

The specification and amended claims, therefore, provide adequate description of the various types of linkers that can be used to conjugate the adduct to the therapeutically active compound. Applicants respectfully note that an inventor "need not, however, explain every detail since he is speaking to those skilled in the art." *In re Howarth*, 654 F.2d 103, 105 (CCPA 1981). As the Federal Circuit has held, "[n]ot every last detail is to be described, else patent specifications would turn into production specifications, which they were never intended to be." *In re Gay*, 309 F.2d 769, 774 (CCPA 1962). Given the disclosure within the present specification, one of ordinary skill in the art would recognize that Applicants were clearly in possession of the invention as of the filing date of the application.

In light of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 102(b)

The Examiner rejected claims 1-10, 12, and 13 under 35 U.S.C. § 102(b) as being allegedly anticipated by Luedtke et al. (*J. Am. Chem. Soc.* 122: 12035-12036 (2000)). The Examiner argues the Luedtke discloses guanidinoglycosides bound to RNA and therefore anticipate Applicants' claimed conjugates.

Applicants respectfully disagree. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." See *Verdegall Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Claim 1, as amended, recites a composition comprising a therapeutically active compound covalently bonded to an adduct of a dialkoxy substance and a guanidinylating reagent. Luedtke relates to a guanidinoglycoside bound to RNA through electrostatic interactions

mediated by the guanidinium groups (see, e.g., Luedtke paragraphs 1 and 2). Luedtke does not, however, disclose covalently bonding a therapeutically active compound to the adduct of a dialkoxy substance and a guanidinuylating reagent as required by the instant claims. Therefore Luedtke does not recite each and every limitation in the claim and cannot anticipate the presently claimed invention.

In light of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 102(b).

CONCLUSIONS

Applicants respectfully assert that the claims are in condition for allowance, which action is hereby requested. The Examiner is invited to telephone the undersigned attorney if such would expedite prosecution.

Please charge the fees for extra claims (8 dependent) to deposit account 06-1050. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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